American Journal of Medical Genetics 61:293–294 (1996)

Letter to the Editor

Midline Field Defects and Hirschsprung Disease

To the Editor:

Recently we saw an infant who had midline defects and Hirschsprung disease, which brought to mind the paper by Jespers et al. [1993] on 2 sibs with similar defects. Those children were born to healthy, consanguineous parents, suggesting autosomal recessive inheritance. The authors concluded that their patients either represented a new entity or were examples of variable expression of Toriello-Carey syndrome [Toriello and Carey, 1988]. We are reporting on our patient to increase knowledge regarding this intriguing combination of malformations.

CLINICAL REPORT

This male infant, who is now 3 months old, was born to a 22-year-old G2, P1 mother after a term uncomplicated pregnancy and labor. Apgar scores were 8 and 9 at one and 5 minutes, respectively, and the birth weight was 3,530 g. The father is 32 years old, and there is no consanguinity between the parents. The mother's first child is a healthy 2-year-old girl by a different union. The father has no other children. There was no known teratogenic exposure during pregnancy except for cigarette smoking. The family history on both sides was unremarkable.

A physical examination soon after birth showed a wide fontanel (10 × 5 cm), unilateral cleft lip and palate (CLP), nose deviated to the left, and apparently low-set ears. There was a simian crease on the left palm with an incomplete one on the right, tapering fingers with hypoplastic nails, absent right fifth toe, and on the left foot the 4th and 5th toes were fused. Routine hematology and chemistry studies and urinalysis were normal. High resolution chromosome analysis showed a normal male karyotype, 46,XY.

By the third day after birth, the child's condition was stable, and he was tolerating breastmilk and feeding well. Therefore, he was discharged to home with plans for a plastic surgery consult for the cleft defects within the week. Later that evening, he was brought back to the emergency department because of persistent vomiting associated with abdominal distension. Radiologic studies of the abdomen suggested lower intestinal (anorectal) stenosis, 3.5 cm in length, producing bowel obstruction. A left colostomy was performed, with biopsies of the sigmoid colon and rectum. The biopsies showed no ganglion cells, consistent with a diagnosis of Hirschsprung disease.

Additional studies were performed at this time to rule out any other undetected anomalies. A renal sonogram did not show any kidney abnormalities, and no central nervous system (CNS) abnormalities were detected by computerized axial tomography (CT scan). However, echocardiogram by 2-dimensional color flow Doppler demonstrated a mild hypertrophy of the right ventricle, and tricuspid regurgitation suggesting right ventricular or pulmonary hypertension and finally, an atrial septal defect (ASD). A skeletal survey was normal, except for the digit anomalies consisting of only 4 toes with a short 4th metatarsal bone on the right, and the entire fifth metatarsal bone and toe missing on the left. The cleft lip was repaired before he was discharged.

We saw him on an outpatient basis when he was 10 weeks old. His OFC and weight were at the 10th and 5th centiles, respectively for age, while his length was at the 25th centile. Eye measurements showed the outer canthal distance to be 7.8 cm, inner canthal distance 2.2 cm, and the interpupillary distance 4.2 cm. All of these measurements were above 2 SDs for age.

In summary, the infant presented here has midline defects, specifically CLP and congenital heart defect, in addition to digit abnormalities. More interestingly, he also has Hirschsprung disease, as was the case with the sibs reported by Jespers et al. [1993]. The absence of microcephaly and corpus callosum abnormalities, and the presence of Hirschsprung disease in those 2 sibs and our patient, may indicate that they represent a new syndrome distinct from Toriello-Carey. On the other hand, it is intriguing that our patient had oligodactyly. We are are aware of 2 further reports by Laurence et al. [1975] and Santos et al. [1988], both of which were on sibs with Hirschsprung disease associated with polydactyly. It is clear that the reporting of additional cases is needed before one can reach an intelligent conclusion on this matter. Of course, the final clarification would be by the delineation of their common molecular basis.

Received for publication May 30, 1995; revision received September 8, 1995.

Address reprint requests to Burhan Say, M.D., H.A. Chapman Institute of Medical Genetics, 5300 E. Skelly Drive, Tulsa, OK 74135.

ACKNOWLEDGMENTS

We thank the parents for their cooperation and Dr. J. Cuadra for referring the family.

REFERENCES

Jespers A, Butinx I, Melis M, Vaerenberg M, Janssens G (1993): Two siblings with midline field defects and Hirschsprung disease. Am J Med Genet 47:299–302.

Laurence KM, Prosser R, Rocker I, Pearson JF, Richards C (1975): Hirschsprung's disease associated with congenital heart malformation, broad big toes and ulnar polydactyly in sibs: A case for fetoscopy. J Med Genet 12:334–338.

Santos H, Mateus J, Leal MJ (1988): Hirschsprung disease with polydactyly, renal agenesis and deafness. J Med Genet 25:204–208.

Toriello HV, Carey JC (1988): Corpus callosum agenesis, facial anomalies, Robin sequence and other anomalies: A new autosomal recessive syndrome? Am J Med Genet 31:17–23.

Burhan Say
Donna P. Smith
H.A. Chapman Institute of Medical Genetics
Tulsa, Oklahoma